MEDICAL PROCEEDINGS

MEDIESE BYDRAES

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REDAKSIONEEL · EDITORIAL

STERFGEVALLE GEASSOSIEER MET ANESTESIE

Fundamentele helderheid is aan die besprekings in verband met sogenaamde ‚anestetiese' sterfgevalle verleen deur hulle op 'n baie akkurater en presieser manier as ‚sterfgevalle geassosier met anestesie' te bestempel—'n nogal veelbeduidende verskil.[1]

Artikel 86 van die Wet op Geneeshere, Tandartse en Aptekers handel oor sterfgevalle onder persone aan wie narkose toegedien is. Hierdie Artikel maak dit duidelik dat sterfgevalle onderwyl persone onder die invloed van plaaslike of algemene verdowingsmiddels is, of waartoe die narkose bygedra het, nie as sterfgevalle ten gevolge van natuurlike oorsake beskou word nie. Die gevolg is dat 'n geregtelike ondersoek, d.w.s. 'n lykskouing gehou moet word in die geval van alle persone wat op hierdie manier sterf. Daar moet egter besef word dat operasies van 'n omvang wat selfs 'n paar dekades gelede heeltemal ongehoord sou gewees het deur moderne anestesie moontlik gemaak is. Temeer, tegniese vorderings het pasiënte wat as 'n swak risiko beskou word en feitlik sterwend is, na die operasietafel gebring en hulle 'n kans gebied wat hulle slegs 'n paar jaar gelede beslis nie sou gehad het nie. Sterfgevalle wat in sulke omstandighede plaasvind, kan derhalwe skaars beskou word as gevalle wat *prima facie* in die openbaar ondersoek behoort te word.

1. Gordon, I. (1941): S-A. Tydskr. Geneesk., **15**, 243.

DEATHS ASSOCIATED WITH ANAESTHESIA

A point of fundamental clarity was introduced into discussions about so-called 'anaesthetic' deaths by describing them more accurately and precisely as 'deaths associated with anaesthesia'—a distinction with a considerable difference.[1]

Section 86 of the Medical, Dental and Pharmacy Act deals with deaths of persons under anaesthetics. This Section makes it clear that deaths whilst persons are under the influence of local or general anaesthetics, or to which the anaesthetic has been contributory, are not deaths from natural causes. The result is that all such deaths must come to public inquiry at inquests. However, it must be appreciated that modern anaesthesia has made possible operations of a magnitude which could not even have been contemplated a few decades ago. Moreover, advances in techniques have brought on to the operating table poor-risk and virtually moribund patients who can now be given a chance of which they were deprived only a few short years ago. Deaths occurring in these circumstances can hardly be regarded as cases which, *prima facie*, require public investigation.

Two things are clear from the history of Section 86.

Public inquiry into deaths embraced by this Section of the Act operates unfairly to anaesthetists. This was, in fact, the considered con-

1. Gordon, I. (1941): S. Afr. Med. J., **15**, 243.

Die geskiedenis van Artikel 86 maak twee dinge baie duidelik.

'n Geregtelike ondersoek na die sterfgevalle waarop hierdie Artikel van die Wet betrekking het, kan onbillik teenoor die narkotiseur wees. Dit was inderdaad die oorwoë gevolgtrekking van die *Komitee insake Sterfgevalle onder Verdowingsmiddels* wat in 1936 deur die Minister van Volksgesondheid aangestel is. Die Komitee was die mening toegedaan dat baie sterfgevalle wat in werklikheid nie anestesie-sterfgevalle was nie, in hierdie land as sodanig beskou word, en dat Artikel 86 van die Wet ,onbillik was teenoor narkotiseurs van wie daar dikwels verlang word om aan 'n sterwende narkose toe te dien met die praktiese sekerheid dat hy (die narkotiseur) later voor 'n lykskouingshof sal moet verskyn. Die gevolg is dat 'n geestestoestand by die narkotiseur geskep word wat 'n neiging het om die veiligheid van die pasiënt in gevaar te stel, want die chirurg word uitermate aangejaag.' Die Komitee het derhalwe aanbeveel dat Artikel 86 gewysig moet word om dit billiker te maak, maar dit is nog nie gedoen nie.

Aangesien die Wet op Lykskouings en die Wet op die Registrasie van Geboortes, Huwelike en Sterfgevalle saam alle sterfgevalle dek, of hulle nou al die gevolg is van natuurlike oorsake al dan nie, is dit moeilik om te begryp wat die doel, indien enige, van hierdie volkome onreëlmatige artikel van die Wet op Geneeshere, Tandartse en Aptekers nou eintlik is.

Onvoldoende wetenskaplike lig word op die oorsake van sterfgevalle geassosieer met anestesie gewerp tydens magistraatslykskouings, en tog is inligting van hierdie aard van groot belang as ons vordering wil maak met preventiewe maatreëls wat hierdie ongelukkige voorvalle sal uitskakel.

Ongeveer 4 jaar gelede het die Raad vir Wetenskaplike en Nywerheidsnavorsing 'n georganiseerde poging aangewend om inligting oor sulke gevalle in te samel. 'n Senior Beurshouer is in Julie 1956 aangestel. Dit was 'n amp wat met die medewerking van die Transvaalse Provinsiale Administrasie geskep is met die spesifieke doel om ondersoek in te stel na die sterfgevalle wat met anestesie en chirurgiese operasies geassosieer is.

Die ondersoek word uitgevoer onder die leiding van dr. O. V. S. Kok, Hoof van die Departement Anestesiologie aan die Universiteit van Pretoria. 'n Eerste stap was om opgawes van sekere toepaslike gegewens in verband met sterfgevalle van hierdie aard verpligtend te maak. Aangesien die verslae van lykskouings nie as bevredigend beskou word nie,

clusion of the *Committee on Deaths under Anaesthesia* (appointed by the Minister of Public Health in 1936). The Committee was of the view that many deaths which were not genuine anaesthetic deaths were regarded as such in this country and that Section 86 of the Act operated 'unfairly to anaesthetists who are frequently called upon to anaesthetize moribund cases with the practical certainty of having to face a public inquest. The result is to create a state of mind in the anaesthetists which tends to endanger the safety of the patient by unduly hurrying the surgeon.' The Committee also recommended that Section 86 should be amended so that it should operate equitably, but this has not yet been done.

Since the Inquest Act and the Births, Marriages and Deaths Registration Act between them adequately cover all forms of death, whether due to natural causes or not, it is difficult to see what purpose, if any, is served by this entirely anomalous section of the Medical, Dental and Pharmacy Act.

Inadequate scientific light has been shed on the causes of deaths associated with anaesthesia as a result of magisterial inquests; yet information of this kind is vital if we are to progress in preventive measures which will avoid these unfortunate incidents.

An organized attempt to collect adequate information about these cases was initiated by the C.S.I.R. some 4 years ago. A Senior Bursar was appointed in July 1956, a post established in conjunction with the Transvaal Provincial Administration for the specific purpose of investigating deaths associated with anaesthesia and surgical operations.

The investigation is being carried out under the direction of Dr. O. V. S. Kok, Head of the Department of Anaesthesia at the University of Pretoria. A first step has been to make compulsory in the Transvaal the return of certain relevant data about deaths of this nature. As inquest proceedings have proved unsatisfactory, the garnering of more comprehensive information by the Bursar will make possible a more satisfactory analysis of the situation.

The submission of returns is compulsory in the Transvaal, but much can be done to assist the investigation if hospitals in other Provinces co-operate on a voluntary basis. It is only by a clear understanding of the truly operative causes of deaths in particular cases that effective preventive measures can be developed.

An adequate educational programme, for undergraduates as well as interns, must be re-

sal die insameling van meer omvattende inligting deur die Beurshouer dit moontlik maak om die toestand beter te ontleed.

Die voorlegging van gegewens is verpligtend in Transvaal, maar veel kan gedoen word om die ondersoek te bevorder as hospitale in ander provinsies op 'n vrywillige basis saamwerk. Slegs as ons 'n duidelike begrip het van die werklike oorsake van bepaalde sterfgevalle sal dit moontlik wees om voorkomingsmaatreëls te ontwerp.

'n Doeltreffende opvoedingsprogram vir ongegradueerdes en interns moet as 'n essensiële onderdeel van die hele onderneming beskou word. Dit is verontrustend om bv. te verneem dat dit vir onlangs gegradueerdes moontlik is om hul internskapstyd te voltooi sonder enige doeltreffende ondervinding in narkose. Dis 'n toestand wat die dringende aandag van die Geneeskundige Raad verg.

Daarbenewens behoort die allerernstigste aandag bestee te word aan die aanbeveling uitgespreek deur 'n Hoofmagistraat in die loop van 'n geregtelike ondersoek na 'n sterfgeval wat met anestesie geassosieer was. Die magistraat wat deur 'n mediese assessor bygestaan is, het onder meer die mening uitgespreek dat alle interns 'n verpligte tydperk van ten minste 'n maand aan narkose moet wy.*[2]

Deskundige narkotiseurs kan nie geskep word met massaproduksie-opvoedingstegnieke nie. Met ewe veel reg kan daar waarskynlik beweer word dat geen tipe mediese praktisyn op hierdie manier opgelewer kan word nie, maar die argument weeg selfs swaarder as dit by opleiding in narkose kom. Sonder die minste aarseling kan daar gesê word dat daar dwarsdeur die land, op die platteland sowel as in die stede, 'n dringende behoefte bestaan aan mediese praktisyns wat so ervare in die toediening van verdowingsmiddels is dat geregtelike ondersoeke na hierdie tragiese ongelukke 'n seldsaamheid behoort te word.

Een van die opvallendste kenmerke wat reeds duidelik blyk uit 'n voorlopige betragting van die ingesamelde gegewens, is die belangrikheid van primêre hartstilstand en die toenemende voorkoms daarvan.[3] Hierdie toestand kom meer dikwels op vroeë leeftyd (tot 10 jaar) voor en ná die leeftyd van 50 jaar. 'n Ophoping van koolsuurgas hou 'n wesenlike gevaar in, want dit dra by tot verhoogde prikkelbaarheid van die hartspier. Hierdie toestand kan ontstaan (tensy spesiale maatreëls getref word om dit te voorgarded as an essential part of the whole undertaking. It is disturbing to learn, e.g. that it is possible for recent graduates to complete their period of internship without any adequate experience of anaesthesia—a situation which requires the urgent attention of the Medical Council.

Moreover, a recent recommendation by a Chief Magistrate in the course of an inquest into a death associated with anaesthesia, invites very serious attention. The magistrate, who was assisted by a medical assessor, expressed the view, *inter alia,* that all interns should do a compulsory period of at least one month entirely devoted to anaesthetics.*[2]

Skilled anaesthetists cannot be created with mass production educational techniques. It is probably true to say that no type of medical practitioner can be produced in this way, but the argument has even greater force in respect of training in anaesthesia. There can be no reservations in stating the urgent case for providing throughout the country, in rural as well as in urban areas, medical practitioners so skilled in the administration of anaesthetics that inquests into these tragic accidents should become a most rare occasion.

One of the striking features which has already become clear from a preliminary survey of the data gathered, is the importance of primary cardiac arrest and its increasing incidence.[3] This condition has a greater incidence in the early years of life (up to 10 years) and after 50 years. Carbon dioxide accumulation is a very real danger because it contributes to increased irritability of the heart muscle. This situation may arise (unless special care is taken to prevent it) during the use of artificial pulmonary ventilation and muscular relaxants, so widely employed in modern anaesthesia.

This dramatic interruption of the action of the heart need not be irreversible, but the methods of treatment of one of the most acute emergencies which can arise, must be adequate and prompt. There are very few cases where

*Die Suid-Afrikaanse Vereniging van Narkotiseurs steun ook hierdie standpunt. Die Vereniging dring reeds 'n hele paar jaar daarop aan dat interns 'n verpligte tydperk van een maand in 'n narkose-departement moet voltooi, so nie, dat hulle ten minste 100 narkoses onder toesig moet toedien voordat registrasie as mediese praktisyn toegelaat kan word.

2. Lykskouing Germistonse Magistraatshof, 10 September 1957.
3. Kok, O. V. S. (1958): S-A. Tydskr. Geneesk., **32,** 180.

*The South African Society of Anaesthetists also supports this view. It has for some years now urged that interns should be required to do a compulsory period of anaesthetics administration for one month or, alternatively that they should be required to administer at least 100 anaesthetics under supervision before registration as a medical practitioner is permitted.

2. Inquest, Germiston Magistrate's Court, 10 September 1957.
3. Kok, O.V.S. (1958): S. Afr. Med. J., **32,** 180.

kom) tydens die toepassing van kunsmatige pulmonêre ventilasie- en die gebruik van spierverslappers wat so dikwels aangewend word in moderne anestesie.

Hierdie dramatiese onderbreking van die hartaksie hoef nie onomkeerbaar te wees nie, maar die metodes vir die behandeling van een van die akuutste noodgevalle wat moontlik kan ontstaan, moet doelmatig wees en dadelik toegepas word. Daar is baie min gevalle waar 'n gesonde hart wat skielik tot stilstand kom, nie weer in werking gestel kan word nie as opwekkingsmaatreëls dadelik toegepas word sodat suurstofvoorsiening aan die lewensbelangrike sentrums met so min vertraging as moontlik hervat kan word.

Die huidige vasberade aanval op die oorsake van die sterftes wat met chirurgiese prosedures geassosieer is, bied die beste hoop om middele te vind vir die vermindering en voorkoming van lewensverlies. Daar word gehoop dat die waardevolle gegewens wat ingesamel word, met verloop van tyd 'n gesonde grondslag sal verskaf vir die hersiening van die betrokke wetgewing sodat pasiënte nie onnodig bang hoef te wees om hulle aan die nodige chirurgiese prosedures te onderwerp nie, en van ewe groot belang, die kalklig van ongeregverdigde publisiteit nie op mediese praktisyns hoef te val nie.

'n Gelyktydige verbetering van die opleiding van ongegradueerdes en interns in die gebruik van verdowingsmiddels het reeds geblyk wenslik en noodsaaklik te wees, en die aandag wat die voorlopige ondersoek op die omkeerbare aard van primêre hartstilstand gevestig het, sal 'n nuttige invloed uitoefen op die instelling van 'n geroetineerde en duidelik omskrewe prosedure om hierdie noodgeval met welslae die hoof te bied.

'n Waardevolle, sorgvuldig georganiseerde en beplande ondersoek is met medewerking van ander dele van die Unie in Transvaal van stapel gestuur. Volledige landswye samewerking sal die versamelde ondervinding van die hele land tot beskikking van die ondersoekers stel, met die gevolg dat dit dan moontlik sal wees om hierdie inligting te vergelyk, te ontleed en tot welsyn van die algemene publiek aan te wend.

a healthy heart, suddenly arrested, cannot be restored if resuscitative measures are taken immediately so that the oxygen supply to the vital centres is restored with a minimum of delay.

The present determined attack on the causes of death associated with surgical procedures offers the best hope of finding ways and means to reduce and prevent loss of life. In the course of time it is to be hoped that the valuable data gathered will provide a sound basis for revising the relevant legislation so that patients are not needlessly frightened out of submitting to necessary surgical procedures and, equally important, that medical practitioners are not brought into the limelight of unwarranted publicity.

A collateral advance in improving undergraduate and intern training in the use of anaesthetics has already emerged as desirable and necessary and the attention which the preliminary survey has focused on the reversible nature of primary cardiac arrest will have a useful influence in stimulating the organization of a routine, clearly defined procedure for dealing successfully with this emergency.

A valuable, carefully organized and planned investigation is under way in the Transvaal, with co-operation from other parts of the Union. More complete nation-wide collaboration will provide the investigators with the accumulated experience of the whole country which can then be collated, analysed and applied for the public good.

OPENBARE BYDRAES OM PASIËNTE NA DIE BUITELAND TE STUUR

Belangrike beginsel- en perspektiefsake word te berde gebring deur die beroep wat die burgemeestersvrou van Somerset-Wes* op die publiek gedoen het om geld by te dra sodat 'n 15-jarige dogter vir 'n ‚slagaargebrek'-operasie na Amerika gestuur kan word.

Die indruk wat onvermydelik deur die koerantpropaganda geskep word, is dat hierdie operasie noodwendig in die buiteland gedoen moet word. Die gepubliseerde inligting laat duidelik blyk dat die pasiënt aan 'n saampersing van die aorta ly en in 'n posisie verkeer om die operasie gratis in hierdie land te laat doen. In die mediese professie in Suid-Afrika word daar allerweë erken dat die chirurgiese herstel van 'n saampersing van die aorta

* *Cape Times*, 26 Junie 1958.

PUBLIC SUBSCRIPTIONS FOR SENDING PATIENTS OVERSEAS

Important matters of principle and perspective are raised by the public appeal made by the Mayoress of Somerset West* for funds to send a 15-year-old girl to America for an operation on an 'artery defect.'

The impression inevitably created in the newspaper propaganda is that this operation must be done overseas. It is clear from the published information that the patient is suffering from a coarctation of the aorta and is in a position to have the operation done in this country without charge. It is well recognized by the medical profession in South Africa that the surgical repair of coarctation of the aorta is a perfectly straightforward procedure

* *Cape Times*, 26 June 1958.

'n volkome eenvoudige operasie is wat deur borschirurge in al die groot stede van die Unie uitgevoer word.

Diegene wat dit kan bekostig, moet natuurlik heeltemal vrygelaat word om hul eie dokters te kies, of daardie dokters nou al in hierdie land of elders is; maar dis 'n heeltemal ander saak wanneer 'n openbare veldtog van stapel gestuur word om geld vir 'n pasiënt se behandeling in te samel. In hierdie geval, en aan die hand van die beskikbare inligting, skyn dit asof daar geen regverdiging is vir 'n beroep op die vrygewigheid van die Suid-Afrikaanse publiek nie, want die betrokke pasiënt kan haar toestand heeltemal gratis hier te lande behandel.

Die operasie vir die herstel van saampersing van die aorta bring nie die gebruik van 'n kunsmatige hart-long-masjien mee nie. Nog minder is oop-hart-chirurgie daarvoor nodig. Tot pas onlangs toe (inderdaad tot 29 Julie van vandeesjaar) was dit miskien geregverdig om 'n ernstig siek pasiënt wat 'n oop-hart-operasie met 'n pomp-oksigenator moes ondergaan, d.w.s. vir 'n prosedure wat langer as 7 minute duur, na die buiteland te stuur. Maar selfs hierdie posisie sal nou in hersiening geneem moet word, aangesien 'n suksesvolle operasie met behulp van 'n kunsmatige hart-long-masjien onlangs vir die eerste keer in Kaapstad uitgevoer is op 'n pasiënt met aangebore pulmonalestenose. (In hierdie geval het die werklike ompad 14 minute lank geduur).

Dit is derhalwe duidelik dat ten gevolge van hierdie deurbarsting aan die tegniese front, byna alle vorms van oop-hart-chirurgie voortaan in die vernaamste stede van die Unie moontlik sal wees.

Die noodsaaklikheid om pasiënte vir oop-hart-chirurgie na die buiteland te stuur, verval dus in 'n baie groot mate.

Voordat daar 'n beroep om geld op die publiek gedoen word, skyn dit vir ons passend te wees dat oorleg gepleeg moet word met diegene wat in staat is om leiding aan die publiek te gee. Die mediese professie was nog altyd gewillig om in sulke gevalle te help. Ons is seker dat 'n onafhanklike komitee van deskundiges op 'n besondere gebied in elke groot stad maar te bly sal wees om die omstandighede van enige geval te oorweeg, om leiding aan die publiek te gee oor die mate waarin daar in ons eie land in die behoeftes van die pasiënt voorsien kan word, en om aan te raai wanneer dit nodig is om 'n pasiënt na die buiteland te stuur.

Temeer, die beroepe om pasiënte wat op 'n heeltemal doeltreffende wyse hier in die Unie behandel kan word, na die buiteland te stuur, moet noodwendig 'n ongustige effek hê op en die vertroue ondermyn van siek pasiënte wat dergelike operasies in Suid-Afrika moet ondergaan—en dis 'n heeltemal ongeoorloofde posisie.

Waar ons hierdie onderwerp te berde bring, is ons hoofdoel nie om enige spesifieke beroep te prejudiseer nie, maar om die aandag te vestig op die skade wat onwetend aangerig kan word deur diegene wie se dade ongetwyfeld uit die edelste beweegredes voortspruit.

which is carried out by thoracic surgeons in all the big centres of the Union.

Those who can afford to do so should clearly be free to choose their own doctors, whether in this country or elsewhere; but the position is quite different when a public campaign is initiated to collect funds for a patient's treatment. In this case, on the information available, there seems no justification whatever for appealing to the charitable impulses of the South African public, as the patient concerned can have expert treatment here for her condition without charge.

The operation for coarctation of the aorta does not involve the use of an artificial heart-lung machine and open heart surgery. Until recently (in fact, 29 July this year) a case could have been made out for sending overseas an acutely ill patient who required open cardiac surgery with a pump oxygenator, i.e. for a procedure which lasts more than 7 minutes. However, even this position must now come under complete review since a case of congenital pulmonic stenonsis was, for the first time, operated on successfully in Cape Town with the aid of an artificial heart-lung machine. (In this case the actual by-pass lasted 14 minutes).

It is therefore clear that as a result of this break-through on the technical front, almost all forms of open heart surgery will henceforth be possible in the main centres of the Union.

For the most part, the need to send overseas cases requiring open heart surgery now also falls away.

Before any public appeal for funds is made, it seems proper that adequate consultation should be sought with those able to guide the public. The medical profession has always been only too ready to assist in this matter. In every centre, an independent committee of experts in the field would, we feel sure, be prepared to consider the particular circumstances of a case and guide the public about the extent to which the situation can be met here, and advise when it is necessary for a case to be sent overseas.

Furthermore, appeals for sending overseas patients who can be treated adequately in the Union, must necessarily have the undesirable effect of shaking the confidence of ill patients awaiting similar operations in South Africa—a wholly unwarranted situation.

Our primary purpose in commenting on the position is not to prejudice any specific appeal but to draw attention to the harm which may unwittingly be done by those whose actions are undoubtedly inspired by noble motives.

SQUAMOUS CARCINOMA OF THE BREAST

REPORT OF A CASE

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A review of the literature indicates that squamous cell carcinoma of the breast is a rare tumour. Deaver and McFarland[1] and Johnson and Lawrence,[2] reported 2 and 4 cases respectively. Haagensen[3] found 2 squamous cell carcinomas among 164 mammary cancers. Foot and Moore[4] give an incidence of 0.5%. Willis[5] gives an incidence of 1%. James and Treip[6] reported 2 cases, and drew attention to 2 recent cases of squamous cell carcinoma seen at the Central Middlesex Hospital, representing the only 2 cases seen in a series of 500 cases of breast tumours.

CLASSIFICATION

Geshickter[7] states that Paget's disease of the nipple, duct cancers and neo-mammary cancers may resemble histologically forms of epidermoid carcinoma found in skin and mucous membranes. Such mammary cancers, however, are readily distinguished from true squamous cell cancers.

There are 3 groups of epidermoid carcinoma:

1. Squamous cell cancer arising in epidermoid cysts.
2. Squamous cell metaplasia with malignant change arising in a fibro-adenoma.
3. Grade IV neomammary cancers (medullary carcinoma) with a scattering of squamous cells.

CASE REPORT

Mrs. A. L., aged 40 years, was admitted to Ward 19 of the Johannesburg General Hospital on 16 November 1956, complaining of a discharge from the left nipple of 1 year's duration. She stated that she never actually saw the discharge, but her underclothing was always wet. This discharge had become more copious and had been blood-stained for the last month. She had had discomfort and shooting pains in the breast for 1 year.

Previous History. Para IV, gravida IV, youngest child 4 years of age. In 1954 she had an amputation of the cervix with an anterior and posterior repair of the vaginal wall.

Examination: Left Breast. The appearance was normal. There was no retraction of the nipple. No tumour could be palpated. The regional lymph nodes were not enlarged, but blood-stained fluid was expressed from the nipple. A diagnosis of an intraduct papilloma was made and on 23 May 1957 a segmental resection was carried out, after dilatation of the affected duct. A frozen section done at operation confirmed the presence of an intraduct papilloma. This opinion was confirmed by paraffin section, the report on which was as follows:

'Sections of this specimen from the left breast, all of which has been embedded, show the presence of large dilated ducts containing eosinophilic debris. In one duct there is a small fragmented mass of epithelium, the appearances of which are suggestive of a small intraduct papilloma. There is no histological evidence of malignancy in the sections examined.'

The patient was discharged from hospital and told to report to the Outpatients' Department for observation. On 6 August 1957 the patient was re-admitted to hospital. She stated that following the previous operation on her breast she was quite well until one month ago. While doing her housework, she suddenly experienced a severe pain in the left breast, which lasted a few minutes. This disappeared, but left her with a dull ache, and she then noticed that she had a hard mass in the breast.

Examination (*6 August 1957*): This revealed a stony-hard mass in the outer, lower quadrant of the left breast, which was not in relation to the previous operation scar. The nipple was not retracted, nor was there any evidence of skin puckering. There was no evidence of lymph node enlargement.

On 8 August 1957 the tumour was excised under general anaesthesia. Examination of the lump, which was situated well below the skin, showed what appeared to be a dilated duct with a small papilloma projecting into it.

A frozen section was done. This showed the presence of many epithelial pearls in the papillomatous projection and portion of the wall. It could not be stated definitely on the section whether this was a squamous carcinoma or squamous metaplasia of the epithelial lining. Consequently, it was decided to close the biopsy site and await the result of the paraffin sections.

On 12 August this report showed the presence of an intraduct keratinizing squamous carcinoma, with some evidence of infiltration into the underlying tissue (Fig. 1). On 18 August a simple mastectomy was carried out. The report on this specimen was a follows:

'The specimen submitted consisted of a simple mastectomy in which there was a recent biopsy scar. Sections were taken from the vicinity of the biopsy scar and of the rest of the breast tissue.

In a section taken of the tissue in the vicinity of the biopsy scar, the histological features were those of a fibro-adenosis in which one or two of the ducts showed well-marked hyperplasia; the epithelium appeared atypical.

Sections of the remainder of the breast tissue showed the presence of fibro-adenosis with cystic dilatation of some of the ducts. No evidence of malignancy was observed in the sections examined.'

On 27 August she was discharged. She was seen every fortnight at the Outpatients' Department, and was well until 18 April 1958, when she stated that she had noticed a small lump in her left axilla 2 days before. It was not tender. She was admitted immediately to Ward 19.

Examination. Two small axillary lymph nodes could easily be palpated in the left axilla. X-ray examination of the chest and the skeleton showed no evidence of any lung or bony metastatic deposits. On 20 April an extensive clearance of the axilla was carried out and the specimen referred for histological examination, the report on which was as follows:

'Sections taken of 2 enlarged lymph nodes from the left axilla showed the presence in one of them of extensive infiltration by a metastatic squamous carcinoma (Fig. 2). The second lymph node showed the presence of reactive hyperplasia and sinus catarrh.'

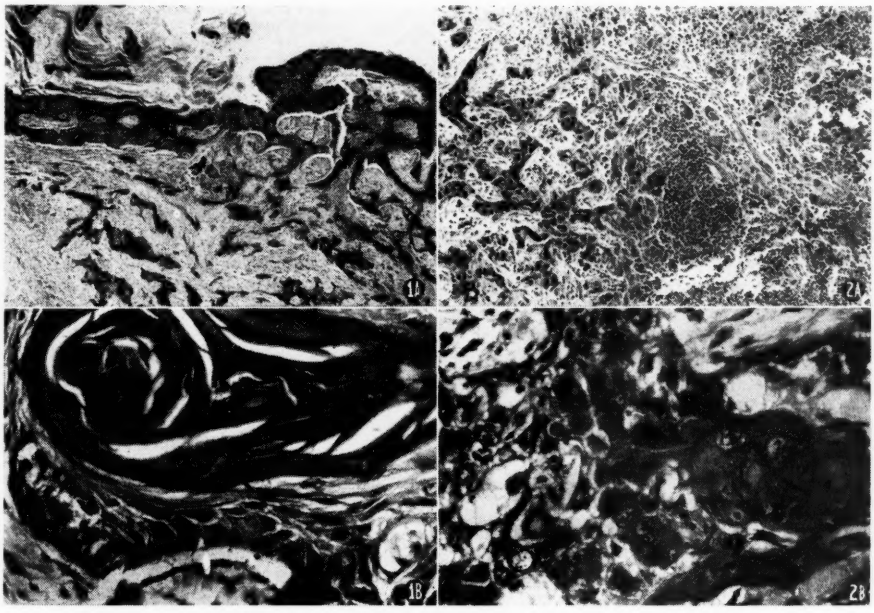

Fig. 1*A*. Portion of duct lined by squamous carcinoma. Note infiltrating nests of squamous carcinoma, some of which shows keratinization in the lower left portion of photograph. (× 38).

Fig. 1*B*. A mass of keratin-formation in a nest of squamous carcinoma and the presence of intercellular bridges between the tumour cells. (× 600).

Fig. 2*A*. Infiltration of an axillary lymph node by squamous carcinoma. (× 150).

Fig. 2*B*. An islet of squamous carcinoma cells with intercellular bridges clearly demonstrated between some of the cells. (× 480).

The patient was discharged from the hospital on 13 May 1958 and will remain under observation at the Outpatients' Department.

During the whole period under review the patient was not given any deep therapy.

DISCUSSION

Epidermoid Cysts.

The view of epidermoid cysts is based on Cohnheim's theory of displaced cell nests. This was upheld by Willis. Geshickter is of the opinion that cysts in the breast are more prone to malignancy than similar cysts elsewhere in the body, and quotes 6 malignant cases among a total of 34 (17%). The degree of malignancy is low.

Pasternach and Wirth[8] found 4 cases of carcinoma among their references to 'cholesteatoma.'

Squamous Metaplasia. Squamous metaplasia has been reported in the ducts and glandular cells of fibro-adenoma of the breast. This metaplasia is thought by some to be due to prolonged oestrogen stimulation. Geshickter draws attention to this occurring in oestrogenic mammary carcinoma in the rat.

Pasternach and Wirth state that physiological squamous metaplasia occurs during pregnancy in the large ducts.

Squamous Cell Carcinoma Arising from Skin.

This is the rarest of the groups and is not a true tumour of the breast itself, but of the skin.

As in the 2 cases reported by James and Treip,[6] there is confirmatory evidence in this case in the epithelium lining several other ducts in the breast tissue around the tumour, that the latter arose as a result of metaplasia of the duct or glandular epithelium. In the remainder of the breast tissue the ducts show the epithelium normally found in a fibro-adenosis of the breast. No evidence was found in the sections examined of the tumour having arisen

1. From an epidermoid cyst undergoing malignant change;
2. From a squamous carcinoma arising from the epidermis or the covering skin or areola;
3. From a nest of squamous cells in a medullary carcinoma.

SUMMARY

A case of squamous carcinoma of the breast is reported. It is felt that the tumour arose from metaplasia of the duct or glandular epithelium.

OPSOMMING

Verslag word gedoen oor 'n geval van skaalvormige karsinoom van die bors.

Daar word gemeen dat die gewas ontstaan het ten gevolge van die metaplasie van die buis- of kliervormige epiteel.

The authors are indebted to the Superintendent of the Johannesburg General Hospital for permission to submit this case for publication.

We should also like to thank Mr. R. Lester Almond for allowing one of us (L. M. D.) to treat this patient who was under his care, and to publish the details.

Our thanks are also due to Mr. M. Ulrich of the S.A. Institute for Medical Research, for the photographs.

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ANAPHYLACTIC REACTION TO ORAL CHLORTETRACYLINE

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Anaphylactic reactions to oral chlortetracycline are not common. The usual side effects on the gastro-intestinal tract, with nausea, vomiting, diarrhoea, glossitis and pruritus, are due to destruction of normal commensals and proliferation of Candida species uninhibited by their biological competitors. True moniliasis, pulmonary and gastro-intestinal, is also sometimes encountered. This usually responds to concurrent or subsequent use of nystatin (myco-

statin). It is usual to prescribe milk or yoghurt and supplementary vitamin B complex to avoid gastro-intestinal trouble of the mild variety. Transient skin reactions with nausea and vomiting occurred in half of 116 patients treated with the high dose of 1 g. 4–8 hourly.[1] Cross sensitization between the 3 tetracyclines has also been reported.

The anaphylactic reaction to chlortetracycline is less common. Bedford[2] reported a severe reaction to 1 gramme orally in a patient with idiosyncrasy to aspirin and penicillin, resulting in oedema and asthma within 2 hours.

CASE REPORT

The patient, a White male aged 39, was seen at Bryanston. He was bitten by a tick at Machadadorp in the Northern Transvaal 7 days before. The next day he felt malaise and he became feverish on the third day. Generalized aches and body pains followed on the fourth day, with sensitivity in the right groin. Despite this he treated himself as a 'flu' with the pharmacist's offering of aspirin, phenacetin, caffeine and Gee's Linctus (Tinct. Scillae, Oxymel Scillae and Tinct. Camph. Co.).

When first seen on the seventh day (9.30 a.m.) his complaints were:

Fever, pain behind the eyes, generalized body pains, constipation and a lump in the right groin.

His temperature was 103° F.; pulse, 90 per minute; the spleen was just palpable. There was a sparse rickettsial rash on the abdomen with one spot on the right palm.

A tick bite was present on the right thigh posteriorly, with corresponding right inguinal lymphadenitis. The palate was red with catarrhal changes in the uvula and the pharynx.

Treatment. Aureomycin 2 capsules (500 mg.) *statim* and 250 mg. 6-hourly with milk, and Surbex (vitamin B complex) one tablet *b.d.*

He took the 2 Aureomycin capsules with one Surbex tablet at 10.30 a.m. Within 15 minutes he felt breathless, his fingers and palms began to swell and he felt as if his face was about to burst. He had a pain at the back of his head, 'as if he were going to have a stroke.' There was numbness about the mouth. All these symptoms came on suddenly, 'within 10 seconds.' He could not clench his hands. The soles of his feet were itchy, as were the interdigital spaces of his toes.

He was seen again at 11.15 a.m., about 20–30 minutes after the development of symptoms.

He had suffused conjunctivae, swollen upper eyelids, a very red face with swollen lips, a raised red rash of confluent, urticarial type on the forearms and the trunk, the latter being brawny and mottled.

His hands were swollen and the fingertips blueish. Respiration, 28 per minute, but no bronchospasm. Temperature, 99.8° F. He was shivering and cold. Blood pressure 130/85 mm. Hg.

He denied previous sensitivity to any of the 3 tetracyclines, nor did he admit to a present or a recent epidermophytosis. (However, on a subsequent examination, fissures between the toes suggestive of epidermophytosis, were seen). He had had Aureomycin 4½ years ago, given by another practitioner for the after-effects of an upper respiratory infection. He was accustomed to alcoholic excess but his last indulgence was mild (one pint of stout and 2 whiskies the previous evening). He had had the pharmacist's mixture already referred to at 6 a.m. and chicken soup at 8 a.m.

Treatment. Intravenous Benadryl (diphenhydramine hydrochloride) 2 ml. (20 mg.). Within half a minute he felt relieved, 'so much so that he felt like weeping;' but after 10 minutes the shivering returned and he was given 80 units corticotrophin gel intramuscularly. Four hours later his temperature rose to 104° F. This was treated with aspirin gr. 10 and tepid sponging.

The next day he was much improved. He had the symptoms only of tick-bite fever and had had 2 bowel actions. There was no rash or oedema. Blood pressure, 120/70 mm. Hg.; pulse, 118 per minute; temperature, 102.6° F. The inguinal glands were much better and less painful. Corticotrophin (40 units) was given. In view of possible necessity, a test instillation of Chloramphenicol ointment in his right eye was done. This did not produce a reaction. By the next day his symptoms were very much improved, so that no recourse was had to Chloramphenicol systemically. The possibility of a previous primary sensitization 4½ years ago to chlortetracycline cannot be excluded.

An interesting feature of this case, apart from the rapidity of onset of anaphylactic symptoms after oral ingestion of gelatin capsules, is the marked regression of the inguinal swelling after one dose only of 500 mg. The other rickettsial symptoms persisted, however, until well after 36 hours later. The exhibition of corticotrophin in severe tick-bite fever has also been reported.[3]

SUMMARY

An exceptionally rare case is reported of anaphylactic reaction to oral chlortetracycline (Aureomycin) capsules. Symptoms commenced 15 to 20 minutes after swallowing the first dose of 2 capsules (500 mg.) in a patient with rickettsial tick-bite fever.

Prompt diphenhydramine (Benadryl) intravenously and corticotrophin gel intramuscularly relieved the acute signs but the allergic reaction persisted for several hours thereafter. There was no history of allergy to any other drugs including the tetracyclines. It is possible that he may have been sensitized by a course of Aureomycin 4½ years before.

OPSOMMING

Verslag word gedoen oor 'n buitengewoon seldsame geval van anafilaktiese reaksie op chloortetrasiklienkapsules (Aureomycin) wat mondeling toegedien is. Die simptome het hul verskyning gemaak binne 15 tot 20 minute nadat die eerste dosis van 2 kapsules (500 mg.) geneem is deur 'n pasiënt wat aan rickettsia-bosluiskoors gely het.

Die vinnige binne-aarse inspuiting van difenhidramien (Benadryl) en die binnespierse toediening van kortikotrofien-jel het die akute tekens verlig, maar die allergiese reaksies het nog etlike ure lank voortgeduur. Daar was geen geskiedenis van 'n allergie vir ander middels, insluitende die tetrasikliene, nie. Dit is moontlik dat die pasiënt gesensitiseer is deur behandeling met Aureomycin 4½ jaar tevore.

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ACUTE POLIOMYELITIS

A STUDY OF THE CLINICAL MANIFESTATIONS OF FIFTY CASES

SEEN AT THE CHILDREN'S HOSPITAL, JOHANNESBURG, DURING THE 1948 EPIDEMIC

WITH SPECIAL REFERENCE TO THE MANAGEMENT IN THE ACUTE PHASE

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(*Continued from p.* 565)

GROUP 2: AFFECTIONS OF THE VITAL CENTRES

i. *Respiratory Centre Group.* It is often very difficult to distinguish symptoms due to the involvement of the respiratory centre from those attributable to paralysis of the peripheral respiratory mechanism. Brown and Baker[37] have clarified the problem. The symptoms come on several days after the onset of cranial nerve pareses and are characterized by shallow respirations with prolonged intervals between them. Finally, prolonged periods of apnoea occur and respiration ceases. These symptoms occur despite strong diaphragmatic and intercostal movement. The patients are extremely anxious and apprehensive. Hypoxia may be present before cyanosis appears and therefore adequate oxygenation is essential, controlled, where possible, by oximetric studies.

The tank respirator or 'iron lung' has been recommended to produce adequate respiratory function in this type of case. The ingenious 'iron lung', devised in 1929 by Drinker and Shaw,[97] is used in cases of poliomyelitis requiring artificial respiration. It attempts to simulate the normal mechanism of breathing by producing pressure changes around the body and functions by alternately producing negative and positive pressures or negative pressures alone. When the pressure surrounding the body is reduced below atmospheric levels air flows into the lungs and distends the alveoli. The inherent elasticity of the lungs and spontaneous expiratory movement result in expulsion of the air during the expiratory phase of respiration.

Children should be started at a (negative) pressure of -10 cm. H_2O. This should never exceed -14 cm. H_2O. If the negative pressure is too great, pulmonary emphysema, pulmonary oedema associated with ruptured alveoli, bronchopneumonia and alkalosis may occur. The rate of respiration is not as important as the height of the negative pressure. For children respiratory rates of 20–30 per minute are sufficient. In the 1952 Copenhagen epidemic tracheotomy was used freely and where necessary artificial respiration was maintained by intermittent positive-pressure res-

piration through a cuffed tracheotomy tube. Tank types of respirators were discarded. Intratracheal positive-pressure ventilation (manual or mechanical) can be kept up continuously and effectively for at least 3 years. The details are well described in Lasser's monograph.[98]

Wesselhoeft[99] described a plastic dome attached to the respirator. It fits over the head of the patient and functions as a resuscitator. Positive pressure is rhythmically produced and forcibly distends the lungs with air. The pressure should not be greater than 8–10 cm. H_2O. It is invaluable when the respirator is not in action for any reason, e.g. nursing care, physiotherapy, mechanical defect, etc.

The respirator is only indicated when respiratory distress is due to diaphragmatic or intercostal paralysis or involvement of the respiratory centre or both. The exact determination of the extent of intercostal or diaphragmatic involvement is important, although the 2 usually co-exist. Splinting of the chest inhibits intercostal movement and therefore tests the efficiency of diaphragmatic movement; upper abdominal splinting inhibits diaphragmatic movement and tests the efficiency of the intercostal muscles. Clinical signs and symptoms of anoxia, inability to cough properly, or count out aloud more than 10 numbers, or 2–3 numbers after expiratory phase, or frequent twitching of the alae nasi or facial muscles in the presence of a clear airway, are definite indications for the use of the respirator.

Bourdillon *et al.*[100] suggested the routine use of spirometric measurements of respiratory function in all cases suspected of respiratory weakness. This method is probably the most sensitive for detecting early impairment and would allow respirator therapy to reach the poliomyelitis patient in the earliest stages of respiratory muscle weakness or respiratory centre involvement. However, these tests require maximum co-operation from an already sick patient.

It is imperative to use the respirator before dyspnoea, cyanosis and the use of accessory muscles of respiration become obvious. Stimson[101] advises the respirator for the patients with breathing difficulty who have gone without sleep for 2–3 nights. They often went to sleep within 5 minutes of being put into the respirator and were very much improved afterwards.

Furthermore, the involved respiratory muscles should be rested as early as possible because of the deleterious effects of fatigue. Unparalysed or weakened muscles whose contraction is necessary to maintain life are overstimulated by hypoxia and hypercapnia and if fatigue sets in, the paralysis will spread and involve more motor neurones, thus setting up a vicious cycle. Since the normal tidal air is about $\frac{1}{8}$ that of the vital capacity, a patient at rest will not show respiratory distress until a very large percentage of his power is lost. It is therefore most important to rest these muscles before this stage is reached.

Most cases are nursed in the prone position, the head only tilted downwards when fluid collects in some part of the respiratory tract. Any constant position is dangerous. It has been shown that the supine position is particularly dangerous owing to difficulty in clearing the pharynx without excessive tilt, and the increased danger of inhalation of gastric contents if vomiting occurs. This applies to respirator as well as bulbar cases.

The percentage of deaths in respirator cases is very high. This is not only due to the large number of cases with overwhelming involvement of the central nervous system that were put into respirators, but also to atelectasis and pneumonia associated with the accumulation of mucus and fluid in the pharynx and bronchi. The prone position is more satisfactory than the supine since it is responsible for a natural tilt of 30° from the carina to the mouth, thereby facilitating drainage. It also obviates the danger of bed sores, since the patient rests on 2 pillows under the chest and thighs. This permits abdominal movement. The patient is also nursed in the accepted positions which facilitate drainage from atelectatic areas.

Experimental and clinical evidence show that several important circulatory changes occur with the application of positive pressure breathing to a patient in a respirator. The circulation is impaired with a fall in blood pressure and decreased cardiac output.[102] These effects are very important when one considers the pathology of poliomyelitic changes on the circulatory and vasomotor centres. Circulatory collapse and cerebral oedema often accompany the respiratory difficulties in poliomyelitis and the increase of either or both can prove fatal. This explains why some cases die soon after being put into the tank respirator. Hyperventilation and underventilation must be prevented. Hyperventilation is easily produced in tank respirators and causes confusion, anxiety and a sense of suffocation, numbness and tingling in the extremities and even tetany. Constriction of the cerebral arteries has been reported and this will lead to further

cerebral anoxia. The peripheral and splanchnic vessels dilate and cause a drop in blood pressure which further aggravates the circulatory state.[103] The only accurate method of estimating hyperventilation is the determination of alveolar carbon dioxide. Underventilation is best estimated by the oximeter.[102] The chief symptoms of hypercapnia are: increased blood-pressure, sweating, especially of the extremities, increased salivation and bronchial secretion, relative bradycardia and mental haziness developing into coma. The symptoms of hypoxia are restlessness, tachycardia, cyanosis and tachypnoea. Special apparatus for the measurement of tidal volume is available in tracheotomized cases.

Disadvantages of the Respirator. (1) It is extremely difficult to nurse a patient in the Drinker iron lung because the whole body is enclosed in the apparatus and switching off the machine, despite the continuous administration of oxygen, causes severe hypoxia.

(2) Many patients are frightened of being placed in it. They become very anxious and struggle against incarceration. Others cannot learn to breath with the machine and if they attempt inspiration during the expiratory phase of the machine or close the glottis during the inspiratory phase, the machine will not assist respiration. On the contrary, fatigue rapidly sets in and pulmonary oedema may ensue.

(3) The collar is made of rubber and chafes the neck.

(4) It is cumbersome, noisy, difficult to transport and expensive.

Despite these disadvantages, the tank respirator has saved numerous lives in poliomyelitis or other neurological diseases (e.g. Guillain-Barré syndrome) affecting the respiratory mechanism. Provided the indications are present and the machine is well controlled, only good can come from its use.

Wilson[104] advised a therapeutic trial if the patient's own respiratory efforts were unsuccessful in maintaining proper oxygenation of the tissues. In those cases with central involvement who still showed signs of hypoxia despite adequate administration of oxygen, the respirator was indicated. More recently Sarnoff *et al.*[105] introduced artificial respiration by electrical stimulation of the phrenic nerve which, in both man and animals, suppresses spontaneous respiration and induces artificial respiration. The function of the respiratory centre is to initiate and co-ordinate respiration, both of which are disturbed when the centre is involved in poliomyelitis. The object of artificial respiration is the suppression of irregular shallow respiration and restoration of regular breathing. Sarnoff *et al.*[105] reported 9 cases on whom this form of therapy was tried. All their pneumotachygrams demonstrated the replacement of irregular respiration by regular breathing. In one case the accompanying hypertension disappeared with the onset of electro-phrenic respiration, while in another restlessness disappeared dramatically. Patients were submitted to this form of therapy for periods varying from 8 hours to many days without ill effects. The advantages of this form of respiration over that of the iron lung are:

1. Nursing is very much easier, since the patient's whole body is not encased within the machine.

2. The stimulation can be increased without the dangers of producing pulmonary oedema or circulatory failure.

3. Cases which have had great difficulty in adjusting their respiration to the respirator rhythm may refuse to be put into the machine.

One of the disadvantages is that continued stimulation of one or both phrenic nerves either indirectly or directly can easily so fatigue the diaphragm that it will eventually become completely paralysed and not contract at all. However, the method is worthy of further trial.

To overcome the nursing and other difficulties associated with the tank respirator, Plum and Lukas[106] used a cuirass respirator in 10 patients with respiratory insufficiency; but this did not prevent or correct respiratory acidosis in 2 acutely ill patients, although partial correction was effected by tank respirators. These, furthermore, produced from 34–100% greater tidal volume of equivalent pressures than did a cuirass respirator on 5 convalescent patients with paralysed respiratory musculature.

They concluded that the cuirass respirator at present is only indicated when one is compelled to use it and when the amount of ventilation produced is physiologically sufficient. It is therefore indicated when bed sores endanger the patients' life or the patient will not submit to the tank respirator and in mild non-progressive cases.

ii. *Circulatory Centre Group.* Marked tachycardia and vasomotor collapse characterized patients with circulatory centre involvement. Whole blood or plasma infusions along with noradrenaline, cortisone or ACTH therapy could be employed, but the outlook was usually hopeless.

Pulmonary Oedema. This produced suffocation as a result of transudation of serous or haemorrhagic fluid from the pulmonary capillaries into the alveoli. It was a prominent finding at necropsy.

Therapy depends on an appreciation of the pathological physiology. The causes of pulmonary oedema in poliomyelitis will therefore be evaluated. Pulmonary oedema may be caused by increased intracranial pressure and intracerebral pathology. The latter etiology was present in cases with involvement of the respiratory centre. Increased intracranial pressure, when present, should be relieved by lumbar puncture, repeated when necessary.

Obstructive lesions in the tracheo-bronchial tree and the post-tracheotomy state readily produce pulmonary oedema. Experimental studies have demonstrated that prolonged pathologically elevated negative intrapleural pressures as well as varied negative or positive pressures in the airway, are followed by congestion and oedema in the lung.[107] The effect of altered lung pressures in the production of lung oedema was further illustrated in Case 24 (bulbar group) who had no cough or expectoration before tracheotomy for laryngeal obstruction, but developed a profuse outpouring of serous and blood-stained fluid into the bronchial tree soon afterwards, dying from pulmonary oedema. The excessive secretion probably occurred because the pulmonary capillaries (formerly adjusted to a positive pressure during expiration against resistance) developed an increased permeability when the positive pressure was suddenly withdrawn. An additional factor altering permeability is the increased pulmonary congestion due to high intrapulmonary negative pressures during the inspiratory cycle, before tracheotomy. These potent causes of pulmonary oedema can be diminished with early prevention and treatment of obstruction of the whole respiratory tract.

The role of the cardiovascular system in the production of pulmonary oedema is important. The lungs may become oedematous in both medical and surgical shock. Lesions of the vasomotor centre and the effect of the respirator on the peripheral circulatory mechanism can induce shock. Therapy of the two conditions is difficult but the blood pressure had to be maintained at all costs by adequate oxygenation, plasma transfusions, noradrenaline and steroid therapy. Visscher[107] suggested that left ventricular failure (the commonest cause of pulmonary oedema) might occur in bulbar poliomyelitis. Heart failure can be due to a combination of several factors, viz. the significant hypertension so common in bulbar poliomyelitis, myocarditis, the anoxia and, in other instances, the shock-like state which still further reduces the blood flow into the coronary circulation.

Several theories have been advanced implicating lesions of the vagi in the production of pulmonary oedema in man, but there is little factual evidence to support this. In animals, however, vagotomy leads to pulmonary oedema, but its exact role in man has still to be evaluated.[103]

The characteristic clinical picture is one of bubbling rales in both lung fields, audible gurgling in the throat and frothy white, pink or blood-stained sputum if expectoration is present. The condition should be suspected when symptoms and signs of hypoxia suddenly develop in bulbar poliomyelitis in the absence of respiratory tract obstruction. Treatment is divided into 2 parts—prevention (already dealt with) and the actual handling of the established condition.

Humidified oxygen therapy under positive pressure (4–5 cm. H_2O) is recommended.[37, 108] Barach[108] recommends 100% oxygen or a mixture of helium and oxygen, whereas Brown and Baker[37] advise mixtures containing up to 40% oxygen in cases with tracheotomy only, since pulmonary oedema is likely if the concentration of oxygen is greater. If a cardiac factor is present, the use of mercurial and digitalis therapy is indicated. Mercurial compounds are probably useful in non-cardiac cases as well. Morphine, however, is contraindicated in bulbar poliomyelitis because of its depressant effect on the respiratory centre, thereby aggravating hypoxia. However, in pulmonary oedema due primarily to cardiac causes, its action is dramatic. Atropine has been recommended to dry up the secretions, but is not very effective. It only makes the secretions more tenacious and difficult to expectorate.

Pulmonary oedema is a very serious threat to life and all efforts to prevent its occurrence should be made.

GROUP 3: COMBINED BULBAR AND SPINAL INVOLVEMENT

The details of therapy in those cases with bulbar involvement alone and those requiring special care because of peripheral respiratory musculature involvement have already been discussed. In this group the therapy of both groups was combined and presented no special features.

The problem of when to remove the patient from the respirator will now be discussed. As soon as the patient is able to use the respiratory musculature to maintain adequate oxygenation with or without oxygen therapy, weaning from the respirator is commenced. At first he should be removed for short periods at a time, 5–10 minutes. The length of the periods and their frequency are increased according to the respiratory efficiency of each patient. This phase of therapy requires much skill on the part of the doctor and maximum co-operation from the patient. No patient should be dismissed from respiratory therapy while there is evidence of clinical or chemical hypoxia at any time during the day.

Table 12 summarizes the causes and therapy of anoxia in poliomyelitis.

The metabolic defects, viz. acidosis and alkalosis, have to be diagnosed and treated accordingly. Hypopotassaemia has been described in 6 patients with bulbar poliomyelitis.[109] Since the hypopotassaemia depresses muscular power, its effect on the respiratory and cardiac musculature only increases the respiratory defect in poliomyelitis and, in some cases, may contribute towards the patient's demise. The administration of 2–3 g. potassium chloride per litre of intravenous fluid daily and then 4 g. orally per day, results in dramatic improvement of muscle contraction in this group. It is therefore essential to watch every seriously ill poliomyelitis patient for this metabolic defect. A normal blood potassium or electrocardiogram does not exclude hypopotassaemia. Potassium should therefore be given routinely in all seriously ill bulbar and bulbo-spinal cases.

SUMMARY

1. The management in the acute phase of poliomyelitis is detailed.

2. The general handling is the same in all the clinical types. Certain symptoms, viz. pain, insomnia, constipation and retention of urine, required symptomatic relief.

3. In the bulbar group constant vigilance is essential.

The various measures and their indications are discussed. Hypoxia must be avoided. Humidified oxygen is essential. The indications for tracheotomy are limited but the procedure can be life-saving. The adequate removal of oral and pharyngeal secretions is imperative. Although the prone position was not used in this series, it is the optimal position.

4. The advantages and disadvantages of the mechanical respirator are detailed. Tracheotomy was routinely employed if the pharyngeal and peripheral breathing musculature were paralysed. The recognition, dangers and treatment of hyper- and hypoventilation consequent on therapy are discussed.

5. The positioning of weak limbs is indicated. Passive movement of the whole body insufficient to cause pain or discomfort was recommended in all cases of acute poliomyelitis. Contractures should never develop with adequate, intelligent care.

OPSOMMING

1. Bestuur tydens die akute fase van poliomiëlitis word beskryf.

2. Die algemene behandeling is dieselfde vir al die kliniese tipes. Sekere simptome, nl. pyn, slaaploosheid, hardlywigheid en die behoud van urine het simptomatiese verligting vereis.

3. In die bulbêre groep is gedurige waaksaamheid absoluut noodsaaklik.

Die verskillende maatreëls en hul indikasies word bespreek. Hipoksie moet vermy word. Bevogtigde suurstof is essensieel. Die indikasies vir tracheotomie is beperk, maar hierdie prosedure kan die lewe van die pasiënt red. Die doeltreffende verwydering van mond- en keelafskeidings is noodsaaklik. Hoewel die plat posisie nie in hierdie reeks gebruik is nie, is dit die bevredigendste.

4. Die voordele en nadele van die meganiese asemhalingstoestel word uiteengesit. Tracheotomie is as roetine-middel toegepas waar die keel- en randstandige asemhalingspierstelsel verlam was. Die herkenning, gevare en behandeling van hiper- en hipoventilasie volgende op terapie word bespreek.

5. Die in posisie stel van swak ledemate word aangedui. Passiewe bewegings van die hele liggaam wat egter nie voldoende was om pyn of ongerief te veroorsaak nie, is aanbeveel in alle gevalle van akute poliomiëlitis. Met doeltreffende, intelligente versorging behoort daar geen verkorting te wees nie.

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NOTES AND NEWS : BERIGTE

Dr. J. C. Gilroy, M.D., M.R.C.P., formerly in practice at 924, Philadelphia Corner, has moved to suite 602 Medical Arts Building, Jeppe Street, Johannesburg. The telephone numbers remain unchanged.

* * *

Mr. Charles Sarkin, M.B., B.Ch. (Rand), F.R.C.S. (Edin.), Orthopaedic Surgeon, has moved to 503, Fifth Floor, Osler Chambers, 215, Jeppe Street (corner of Delvers Street), Johannesburg. (Telephones: *Rooms*: 23-2003; *Residence*: 41-1750).

Mnr. Charles Sarkin, M.B., B.Ch. (Rand), F.R.C.S. (Edin.), Ortopediese Chirurg, het sy spreekkamers verander na Vyfde-vloer 503, Osler-gebou, Jeppestraat 215 (hoek van Delversstraat), Johannesburg. (Telefone: *Spreekkamers*: 23-2003; *Woning*: 41-1750).

* * *

100 MILLION ELECTRON VOLTS AGAINST CANCER

Westdene Products (Pty.) Ltd. (Essanby House, Johannesburg), announce that a new film *100 Million Electron Volts Against Cancer* (Dr. A. Wander, S.A.) has been added to their library and will be loaned on application to their Public Relations Department, P.O. Box 7710, Johannesburg.

The film deals with the roentgentherapy of cancer and its main purpose is to show physicians, who are little acquainted with radiology, the most recent advances made in the field of roentgentherapy.

The working methods and applications of the X-ray generators, from the simple roentgen tube to the betraton, are reviewed and explained by means of trick drawings and selected examples. The pictures of cell divisions of normal tissues and of tissues damaged by radiation, taken by time lapse photography, deserve special mention.

The film is in black and white, 16 mm. sound, and runs for 45 minutes. It was awarded a special distinction at the Biennial Show in Venice, in the category of *Scientific Films*. It will be of interest to all medical practitioners.

* * *

Dr. J. T. Hayward-Butt, F.F.A.R.C.S., Senior Lecturer in Anaesthetics at the Medical Faculty of the University of Natal, is proceeding overseas to take up his appointment of Assistant Professor of Anesthesiology at the State University of Iowa, Iowa City, U.S.A. As a consequence, he will be withdrawing from private practice.

He has been invited by the Society of Anaesthesiologists of Italy, to read a paper at the International Congress, on *Relaxants*, at Venice, and to sit on the Curare Mortality Panel. Following visits to centres in Switzerland, France, Belgium and the United Kingdom, he will undertake a short lecture tour of the East Coast of North America and Canada, before taking up his duties.

* * *

South African practitioners visiting the United Kingdom will be interested in the colour television facilities which have been made available by Smith, Kline and French, London.

Colour television programmes will be featured at the following meetings this year:

Postgraduate Medical School, Hammersmith, London: *19–20 September 1958.*

Anatomical Society of Great Britain Annual Meeting at Guy's Hospital, London: *28 November 1958.*

British Medical Association Clinical Meeting at Southampton: *5–6 December 1958.*

LILLY MEDICAL RESEARCH FELLOWSHIPS

Fourteen physicians from 7 Latin-American countries, Australia, India, New Zealand, the Republic of the Philippines, Scotland, and the Union of South Africa were guests of Eli Lilly & Company on 15, 16 and 17 May 1958. All the lilly guests have been active in medical teaching institutions or in private practice in their native countries and are engaged in postgraduate medical studies in the United States under fellowships provided by Eli Lilly & Company.

The Lilly Foreign Educational Fellowship Programme, which sponsors physicians from all areas of the free world who wish to come to the United States to further their medical studies, was established shortly after World War II. The aim of the fellowship programme is to promote a better understanding and to establish closer ties between members of the medical profession in the United States and other countries and to contribute to postgraduate medical education. Physicians selected to participate in the fellowship programme are chosen with the help of fellow members of the medical profession in their home country. While in the United States, they study in the medical college or institution of their own selection. Their studies may be in general medicine and its related fields or any of the medical specialities. One hundred and one physicians have completed their postgraduate training in the United States under the Lilly Fellowship Programme since 1945.

Dr. W. du T. Naudé (*right*), the Lilly Medical Research Fellow from the University of Cape Town, chatting with Dr. F. B. Peck, Sr., Director of the Lilly Medical Research Co-operation Division, during a visit to Indianapolis in May this year.

Each year before their return to their native land, the Lilly Foreign Fellows and their wives are invited to visit the Lilly research and manufacturing facilities in Indianapolis. The 3-day tour of Lilly operations includes a visit to the research facilities and a first-hand inspection of the research projects being carried out by the company. A visit is also made to the Lilly Laboratory for Clinical Research at Indianapolis General Hospital, as well as a tour through the manufacturing facilities at the McCarty Street and Kentucky Avenue plants and the Biological Laboratories at nearby Greenfield, Indiana. An interesting sidelight of their trip was a visit to the famous Indianapolis Motor Speedway. This famous track is the home of the 500 Mile auto speed and endurance classic which is held once each year on 30 May. The visiting physicians observed pre-race practice trials and the preparation of the many cars being entered in the international speed classic.

The 1958 Lilly Foreign Fellows and their wives who visited Indianapolis were: Dr. Adolpho Barcellini, *Brazil*; Dr. D. W. Beaven, *New Zealand*; Dr. Alonso Cortés, *Colombia*; Dr. Leslie James Park Duncan, *Scotland*; Dr. Gerardo E. Espinosa S., *Cuba*; Dr. Enrique López C., *Chile*; Dr. Robert F. Mahler, *Scotland*; Dr. W. du T. Naudé, *Union of South Africa*; Dr. Eduardo Ramírez, *Peru*; Dr. Alfonso Rivera, *Mexico*; Dr. Carlos Sierra Andino, *Honduras*; Dr. Kamta Prasad Sinha, *India*; Dr. John Barrymore Stokes, *Australia*; Dr. José G. Tamayo, *Republic of the Philippines*.

Dr. Naudé (the 1957 South African Lilly Fellow) is carrying out a programme of virus research at the California Institute of Technology, Pasadena, California. He will return to the University of Cape Town at the end of his Fellowship.

PREPARATE EN TOESTELLE

DEANER ('N VOORLOPER VAN ASETIELCHOLIEN)

Deaner is 'n heeltemal nuwe middel, en is nie verwant aan enige molekule wat tot dusver in die geneeskunde gebruik is nie.

Terwyl dit onder geeneen van die gebruiklike geneesmiddel-klassifikasies ressorteer nie, is dit van belang om daarop te let dat die beste manier om dit te beskryf miskien sou wees om dit 'n biochemiese stof te noem, want dit is die voorloper van asetielcholien. Van groter belang is egter die feit dat *Deaner*, in teenstelling met cholien, metacholien of asetielcholien self, in staat is om die bloed-brein-versperring te oorbrug wanneer dit binne-sels in brein-asetielcholien verander word. Dit skyn asof dit dan die middel se funksie is om 'n ‚psigiese energieverwekker' of 'n ‚biochemiese verbetermiddel' te word.

Dit is beslis *nie* 'n kalmeermiddel nie, want dit verwek energie. Dit het geen simpatomimetiese effek en dit is nie 'n sentrale opwekmiddel nie, want groot dosisse kan met slapenstyd geneem word sonder dat dit die nagrus versteur. Derhalwe kan dit nie saam met efedrien, amfetamien en dergelike middels geklassifiseer word nie.

Daarbenewens word daar verklaar dat dit 'n ontstekingsbestrydingseffek het en dat dit ook van waarde is in gevalle van schisofrenie, maar alleen op 'n langtermyngrondslag.

Die toksisiteit is nul. In uiters uitgebreide proefnemings met diere waar 100 (of meer) keer meer as die terapeutiese dosis oor lang tydperke gebruik is, is geen enkele gevaarlike newe-effek waargeneem nie. Insgelyks het 1,000 menslike vrywilligers normale en groot dosisse geneem met geen nadelige gevolge behalwe die volgende nie:

(*a*) In die geval van te groot dosisse:

i. 'n Gespannenheid af en toe in die nek-, kaak- en vierkopspiere;

ii. verbygaande pruritus van die vel of kopvel;

iii. af en toe 'n geringe mate van slaaploosheid en houdingshipotensie; en

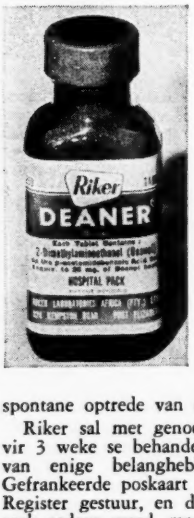
(*b*) In gevalle waar die dosis te vinnig vermeerder is:

i. 'n Dowwe agterkophoofpyn vroeg tydens terapie; en

ii. hardlywigheid.

Die kontra-indikasies is beperk tot grand mal-epilepsie alleen, want 'n geringe vermeerdering van die aanvalsyfer word gerapporteer.

Toestand	*Welslae Behaal*
Hoofpyn (insluitende migraine)	70%–80%
Chroniese Uitputting, Neerslagtigheid, Lusteloosheid	Meer as 70%
Besorgdheid	'n Hoër welslaepersentasie as met kalmeermiddels
Kalmeermiddels in te groot dossise ..	Hoogs suksesvol
Epilepsie	Heilsame effekte oor die algemeen in gevalle van psigomotoriese epilepsie en petit mal.
Spastiese hardlywigheid, Slymdikdermontstekking	'n Hoë mate van welslae
Gedragskwale by kinders, enurese, ens...	Besonder doeltreffend.



Dosis: Aanvanklik 25 mg. (1 tablet) wat na 7 dae tot 2 en dan tot 3 vermeerder word. Dit word as 'n enkele dosis in die oggend geneem.

Kinders het oor die algemeen tussen 12.5 tot 75 mg. per dag nodig, hoewel dosisse van soveel soos 90 mg. per dag in verdeelde dosisse soms toegedien kan word, aangesien sommige kinders groter dosisse as volwassenes moet kry.

Terwyl die middel 2-3 weke nodig het om sy volle effek uit te oefen, is daar geen terugslag wanneer *Deaner*-terapie gestaak word nie. Dit word gewoonlik teweeggebring deur die spontane optrede van die pasiënt self.

Riker sal met genoeë 'n monster wat voldoende vir 3 weke se behandeling is, gratis tot beskikking van enige belanghebbende geneesheer stel. 'n Gefrankeerde poskaart word aan alle dokters in die Register gestuur, en dit kan gebruik word as aansoek gedoen word, maar 'n brief sal ook voldoende wees.

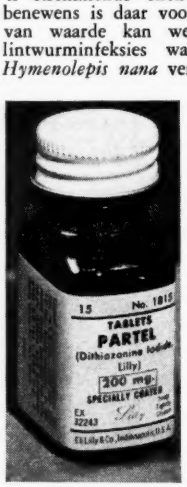
Deaner is 'n verdere oorspronklike navorsingsproduk van Riker, en is verkrygbaar van Riker Laboratories Africa (Pty.) Ltd., Posbus 1355, Port Elizabeth.

PARTEL

(DI-TIASANIENJODIED, LILLY)

Beskrywing: *Partel* is 3,3′-di-etieltiadikarbosianienjodied. Dis 'n nuwe breë-spektrum-wurmmiddel wat, ná mondelinge toediening, hoogs doeltreffend vir die bestryding van 4 van die mees algemene helminte en ten minste gedeeltelik doeltreffend teen 3 ander is.

Indikasies: Uitgebreide kliniese proefnemings het bewys dat *Partel* doeltreffend is teen trichuriase, ascariase, strongiloidiase en enterobiase, en dat dit 'n stremmende effek op haakwurms het. Daarbenewens is daar voorlopige bewyse dat *Partel* ook van waarde kan wees by die behandeling van lintwurminfeksies wat deur *Taenia saginata* en *Hymenolepis nana* veroorsaak word.



Partel is doeltreffend vir die behandeling van enkele en meervoudige helmintinfeksies, sowel as ligte of ernstige besmetting met vatbare nematodes. Dit is reeds met welslae vir die massa-behandeling van besmette groepe gebruik.

Volgende op die verdrywing van hul wurmlas, toon pasiënte wat *Partel* ontvang gewoonlik dadelik 'n kliniese verbetering. Hulle diarree word stopgesit, hul eetlus keer terug, hul gewig neem toe, en bloedarmoede en eosinofilie verdwyn.

Pasiënte wat met *Partel* behandel word, het geen lawemente, of purgeer- of lakseermiddels nodig nie. Dis ook nie nodig vir hulle om te vas of 'n spesiale dieet te kry nie. Die middel word goed verdra. Newe-effekte is 'n seldsaamheid, en as hulle wel voorkom, is hulle lig en van 'n verbygaande aard.

Gewone Dosis: — *Kinders*: 20 pond tot 60 pond, 100 mg. per 10 pond liggaamsgewig, in verdeelde dosisse, per dag gedurende 5 dae.

Volwassenes en Kinders wat meer as 60 Pond Weeg:— 200 mg. 3 maal per dag gedurende 5 dae.

Hoe dit Beskikbaar Gestel Word: *Partel* (Ditiasanienjodied, Lilly) word verskaf in die vorm van spesiaal versuikerde tablette van 100 en 200 mg. in pakkies van 15 en 500.

CELONTIN

'N NUWE ANTI-STUIPTREKKINGSMIDDEL

Ter aanvulling van hul reeds gevestigde anti-stuiptrekkingsmiddels *Epanutin* en *Milontin* het Parke, Davis Laboratories (Pty.) Ltd. nou 'n nuwe anti-stuiptrekkingsmiddel, *Celontin*, beskikbaar gestel om doeltreffende behandeling van die talle uiteenlopende manifestasies van epilepsie moontlik te maak.

Beskrywing: Celontin is 'n heterosikliese anti-stuiptrekkingsverbinding wat vir die eerste keer in die laboratorium van Parke, Davis & Company gesintetiseer is. Die chemiese beskrywing daarvan is soos volg: N-metiel-a, a-metielfenielsuksinimied. Die breë spektrum van anti-stuiptrekkingsbedrywigheid wat met *Celontin* waargeneem is, het die vermoede laat ontstaan dat die kliniese aanpasbaarheid daarvan van 'n groot omvang is.

Indikasies: Celontin word spesiaal aangedui vir die behandeling van psigomotoriese epilepsie—die tipe vallende siekte wat dikwels hardnekkige weerstand teen behandeling met ander anti-stuiptrekkingsmiddels bied. Daar is ook dikwels bevind dat *Celontin* van waarde is vir pasiënte wat aan petit mal ly, en wie se aanvalle nie deur ander middels gekontroleer kan word nie. Wanneer 'n pasiënt aan sowel grand mal- as petit mal-epilepsie ly, kan die beheer van die petit mal-deel by sommige pasiënte aanleiding gee tot 'n verergering van die grand mal. Geen vermeerdering van die voorkoms of erns van grand mal-aanvalle het egter gelyktydig met *Celontin*-terapie voorgekom nie.[1]

In 'n gepubliseerde verslag oor die behandeling van 54 pasiënte, 'n hoë persentasie van wie aan hardnekkige petit mal-aanvalle gely het, het *Celontin* 'n goeie anti-stuiptrekkingseffek gehad.[2] In 'n dergelike studie met 72 pasiënte is daar tot die gevolgtrekking geraak—aan die hand van die aansienlike vermindering van die aantal aanvalle—dat *Celontin* die verkieslike middel vir die behandeling van petit mal is.[3] Die gemiddelde dosis vir hierdie groepe was 0.9 tot 1.2 g. (3–4 Kapseals) per dag.

1. Cordoba, E. en Strobos, R. (Bowman-Gray-skool van Geneeskunde): Moet nog gepubliseer word.
2. Zimmerman, F. en Burgemeister, B.: *Use of N-methyl-a, a-methylphenylsuccinimide in Treatment of Petit Mal Epilepsy,* Arch. Neurol. Psychiat., **72,** 720, 1954.
3. Zimmerman, F. en Burgemeister, B.: *Drugs Used in Treatment of Patients with Petit Mal Epilepsy,* J.A.M.A., 1957, 1194, 1955.

In 'n ander groep bestaande uit 15 pasiënte wat aan psigomotoriese epilepsie gely het, is daar waargeneem dat *Celontin* opmerklike beskerming teen aanvalle verleen het. *Celontin*-terapie is gevolg deur algehele beheer in 3 gevalle, praktiese beheer (vermindering van die aanvalle met tussen 80 en 90%) by 3, en gedeeltelike beheer (vermindering van die aanvalle met tussen 5 tot 79%) by 6. Met ander woorde, die toestand van 12 van die 15 pasiënte is verbeter.

Dosis en Toediening: Die aanbevole aanvanklike dosis is een Kapseal (0.3 g.) per dag gedurende die eerste week. Indien nodig, kan die dosis daarna by tussenpose van 'n week met een Kapseal per dag per week vermeerder word gedurende die 3 daaropvolgende weke, totdat 'n daaglikse maksimumdosis van 4 Kapseals (1.2 g.) toegedien word. Aangesien die terapeutiese effek nie dieselfde by alle pasiënte is nie, behoort terapie met *Celontin* aangepas te word by die individuele behoeftes van iedere pasiënt.

Newe-effekte: Onder die newe-effekte wat *Celontin*-terapie af en toe vergesel, kan daar melding gemaak word van lomerigheid, duiseligheid, koördinasiesteuring, senuweeagtigheid en braking. Die mees gewone newe-effekte is koördinasieversteuring en lomerigheid. Hulle kan egter in die reël gekontroleer word deur die dosis te verminder.

Inligting i.v.m. Verpakking: *Celontin* is verkrygbaar in die vorm van Kapseals (0.3 g.), in bottels van 50.

PREPARATIONS AND APPLIANCES

DEANER (ACETYLCHOLINE PRECURSOR)

Deaner is an entirely new drug, unrelated to any molecule which has previously been used in medicine.

While it fits into none of the usual drug classifications, it is of great interest to note that it is most nearly describable as a biochemical substance, since it is the precursor of acetylcholine. More important, *Deaner* (unlike choline, methacholine or acetylcholine itself) is able to cross the blood: brain barrier, when it is converted intracellularly into brain-acetylcholine. Its function then seems to become that of a 'psychic energizer' or 'biochemical corrective'.

Certainly, it is *not* a tranquillizer, since it energizes. It has no sympathomimetic action and is not a central stimulant, since large doses can be taken on retiring without impairment of sleep; therefore it cannot be classified with ephedrine, amphetamines and the like.

Additionally, it is stated to have an anti-inflammatory action, and is also of value in schizophrenia, but on a long-term basis only.

Toxicity is nil, no single dangerous side effect having been elicited in the most extensive animal experiments using 100 and more times the therapeutic dosage for long periods. Similarly, 1,000 human volunteers have taken normal and large doses with no ill-effect except for:

(*a*) In over-dosage:

i. Occasional tenseness in neck, masseter or quadriceps muscles;

ii. Passing pruritus of skin or scalp;

iii. Rarely, insomnia, postural hypotension of mild degree; and

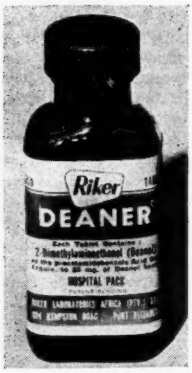
(*b*) In too rapid increase of dosage:

i. Dull occipital headache early in therapy;

ii. Constipation.

Contra-indications are limited to grand mal epilepsy only, some increase in seizure rate having been reported.

Condition	*Success Rate*
Headache (including migraine)	70%–80%
Chronic fatigue, Depression, Lassitude	Over 70%
Anxiety	Better percentage success than with tranquillizers.
Over-dosage with tranquillizing drugs	Highly successful
Epilepsy	Beneficial effects generally, in psychomotor epilepsy and in petit mal
Spastic constipation, Mucous colitis	High success rate
Behavioral disorders in children, enuresis, etc.	Very effective.



Dosage: Initially 25 mg. (1 tablet), increasing to 2 after 7 days and then 3, taken together as one dose in the morning.

Children require from 12.5 to 75 mg. daily on average, though doses up to 90 mg. daily, in divided dosage, are sometimes necessary as some children require larger doses than adults.

While it takes 2-3 weeks to develop its effect, there is also no let-down when *Deaner* therapy is discontinued, which is usually brought about through spontaneous action by the patient himself.

Riker gladly offer 3-weeks trial courses free of charge to any interested medical practitioner. A reply-paid postcard is being sent to all doctors on the Register, and this can be used for application, or a letter will also suffice.

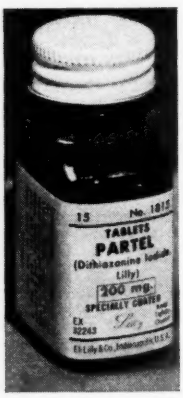
Deaner is another Riker original research product, available through Riker Laboratories Africa (Pty.) Ltd., of P.O. Box 1355, Port Elizabeth.

PARTEL

(DITHIAZANINE IODIDE, LILLY)

Description: *Partel*, 3,3'-diethylthiadicarbocyanine iodide, is a new broad-spectrum anthelmintic which is highly effective on oral administration against 4 of the most common helminths and at least partially effective against 3 others.

Indications: Extensive clinical studies have shown *Partel* to be effective in trichuriasis, ascariasis, strongyloidiasis and enterobiasis and to have inhibitory effect against hookworm. In addition, preliminary evidence suggests that *Partel* may be of value in the treatment of tapeworm infections caused by *Taenia saginata* and *Hymenolepis nana*.



Partel is effective in single and multiple helminthic infections and in light and heavy infections of susceptible nematodes. It has been used successfully in the mass treatment of infected groups.

Following elimination of their worm burden, patients receiving *Partel* usually show immediate clinical improvement such as termination of diarrhoea, return of appetite, gain in weight and elimination of anaemia and eosinophilia.

Patients treated with *Partel* do not need enemas, purgatives, laxatives, fasting or special diets. The drug is well tolerated; side effects are infrequent, mild and transient.

Usual Dosage: *Children*: 20 lb. to 60 lb., 100 mg. per 10 lb. body weight, in divided doses, per day for 5 days.

Adults and children over 60 lb.: 200 mg. 3 times daily for 5 days.

How Supplied: *Partel* (Dithiazanine Iodide, Lilly) is supplied in specially coated tablets of 100 and 200 mg., in packages of 15 and 500.

CELONTIN

A NEW ANTICONVULSANT

Supplementing their established anticonvulsants, *Epanutin* and *Milontin*, Parke, Davis Laboratories (Pty.) Ltd., have introduced *Celontin*, a new anticonvulsant to assist in providing adequate coverage of many of the varied manifestations of epilepsy.

Description: Celontin is a heterocyclic anticonvulsant compound first synthesized in the laboratories of Parke, Davis & Company. The chemical description is: N-methyl-a, a-methylphenylsuccinimide. The broad spectrum of anticonvulsant activity observed with *Celontin* suggests a wide range of clinical applicability.

Indications: Celontin is specially indicated for the treatment of psychomotor epilepsy, the form of epilepsy often refractory to treatment with other anticonvulsants. *Celontin* has also frequently been found to be of value in patients suffering from petit mal, whose attacks were not controlled by other drugs. When a patient has combined grand mal and petit mal epilepsy, control of the petit mal component in some patients may tend to agravate the grand mal. However, no increase in incidence or severity of grand mal attacks has been found to accompany *Celontin* therapy.[1]

In a published report on studies with 54 patients, a high proportion of whom had intractable petit mal seizures, *Celontin* exhibited good anticonvulsant activity.[2] In similar studies with 72 patients, it was concluded on the basis of a high standard of seizure reduction, that *Celontin* is a drug of choice for petit mal.[3] The average dosage for these groups was 0.9 to 1.2 g. (3–4 Kapseals) per day.

In another group consisting of 15 patients with psychomotor epilepsy,[3] *Celontin* was seen to confer measurable protection against seizures. *Celontin* therapy was accompanied by complete control in 3 patients, practical control (80–99% seizure reduction) in 3, and partial control (5 to 79% seizure reduction) in 6, thus providing improvement in 12 of the 15 patients.

Dosage and Administration: The suggested initial dosage schedule is one Kapseal (0.3 g.) per day for the first week. If required the dosage may be increased thereafter, at weekly intervals, by one Kapseal, per day, per week, for the 3 weeks following, to a maximum daily dose of 4 Kapseals (1.2 g.). As the therapeutic effect may vary amongst patients, therapy with *Celontin* should be individualized according to the needs of each patient.

Side Effects: Side effects which have occasionally been reported to accompany *Celontin* therapy include drowsiness, dizziness, ataxia, nervousness, vomiting. The commonest side effects reported are ataxia and drowsiness. These side effects can usually be controlled by reducing the dosage.

Package Information: Celontin is available in Kapseals (0.3 g.) in bottles of 50.

1. Cordoba, E. and Strobos, R. (Bowman-Gray School of Medicine): *To be published.*
2. Zimmerman, F. and Burgemeister, B.: *Use of N-methyl-a, a-methylphenylsuccinimide in Treatment of Petit Mal Epilepsy,* Arch. Neurol. Psychiat., **72,** 720, 1954.
3. Zimmerman, F. and Burgemeister, B.: *Drugs Used in Treatment of Patients with Petit Mal Epilepsy,* J.A.M.A. 1957, 1194, 1955.